The Healthy Uterus

Introduction

The Müllerian ducts become the uterine tubes, uterus, and upper third of the vagina. In this lesson, we do not discuss the cervix (the distal uterus' transition to the vagina) or the upper third of the vagina. We discuss those in Female Reproduction #4: *Cervix and Vagina*. At first glance, it might seem odd to have categorized the Müllerian ducts as a functional unit only to separate their adult structures. If looking at the system from an embryological standpoint, that assumption would be correct.

But here's the thing. If an oocyte is fertilized (Female Reproduction #5: *Fertilization, Implantation, and Early Embryogenesis*), separating the adult structures makes A LOT of sense. The uterine cycle is closely related to the ovarian cycle—estrogen causes the uterine endometrium to proliferate; progesterone causes it to swell with secretions. If there is no fertilization, the oocyte and its corona radiata are swept out of the uterus and expelled. The progesterone wanes, and the endometrium sloughs off, ending in menstruation. But if the oocyte is fertilized (which takes place in the uterine tubes), the embryo will implant in the uterus to develop into a fetus. The journey of the fertilized oocyte ends at the body of the uterus. The cervix and vagina play a role in delivery, but not for nine more months.

Thus, we're approaching the subject with that mindset—the uterine tubes and body of the uterus as one functional unit and the cervix and vagina as another. And just as uterine and ovarian structures overlapped somewhat in the last lesson, so too will some of the cervical and vaginal structures overlap in this lesson. Finally, we use this lesson to discuss the uterine ligaments. We intentionally assigned the ovary, ovarian vessels, and ovarian ligaments to the last lesson to not conflate the ovarian ligaments with the uterine ligaments you will learn in this lesson.

So this lesson encompasses the uterine ligaments (external anatomy), uterine vasculature (including the anastomoses between the uterine and ovarian arteries and between the uterine and vaginal arteries), uterine layers (endometrium, myometrium, and "perimetrium"), and uterine cycle (and its correlation to the ovarian cycle) and then closes with an approach to abnormal uterine bleeding and examples of some of the structural uterine diseases that aren't cancer.

The Uterine Ligaments

The **uterus** is divided into the fundus (the top), the corpus (the body), and the cervix (the exit). The external anatomy of the uterus is best understood by way of the uterine ligaments—their origins, attachments, and functions.

The **ovary** is held in place by the suspensory ligament of the ovary (connects the ovary to the abdominal sidewall) and the ovarian ligament (shared between the ovary and the uterus). The ovarian ligament holds the ovary in place relative to the uterus but doesn't help the uterus's position in the pelvis. The gubernaculum creates the ligament of the ovary by adding an anchor point to the Müllerian duct. The gubernaculum then continues to the inside of the labioscrotal swelling.

Thus, the **top of the uterus** is held in place by that continuation of the gubernaculum to the inside of the anterior pelvic wall, by what is called the **round ligament**. The normal position of the uterus is to lay over the bladder, folding anteriorly, held down and forward by the round ligament.

Three ligaments hold the uterine cervix in place—the pubocervical ligament, uterosacral ligament, and transverse cervical ligament. These three ligaments come in bilateral pairs, but we describe only one side of the body, assuming that you understand that what happens on the left also happens on the right.

We learned previously that the suspensory ligament of the ovary carries blood vessels, lymphatics, and nerves to the ovary, and the transverse cervical ligament does the same for the uterus. All the other ligaments are fibrous bands that provide support alone. We have discussed the ovarian ligament, the round ligament, and the transverse cervical ligament. The remaining ligaments are also used for structural support of the uterus.

The **uterosacral ligament** is the posterior ligament, connecting the uterus to the sacrum (utero-sacral), whereas the **pubocervical ligament** is the anterior ligament, connecting the cervix to the pelvis (pubo-cervical). These, like the round ligament, serve only to hold the uterus in place and become very important in pelvic prolapse (which we address in Clinical Sciences in detail and we touched on in Renal with urinary incontinence).

Those structures we just named are not true ligaments because they do not connect two bones. However, as you saw in GI and the Ovary lesson, ligaments can also be "things I can see in the abdomen and pelvis." Clinically useful when performing surgery, but educationally frustrating when trying to explain what these things are. The **broad "ligament"** is the greatest offender of nomenclature. It isn't a ligament; it is "uterine mesentery." If there were no uterus, there would be a male pelvis—just a bladder and a sigmoid colon. The mesothelium of the peritoneal cavity would line the top of the bladder and the front of the sigmoid colon. The uterus develops "up" from the space in front of the sigmoid colon, behind the bladder, above the rectum, and beneath the peritoneal cavity. The rectum never sees any peritoneal mesothelium in either sex. But the uterus develops "up, and up against" the peritoneal cavity above the rectum, pushing the peritoneal cavity around, as all organs do. The peritoneal cavity accommodates the developing uterus and ovaries, including their blood vessels, lymphatics, nerves, and the other "ligaments" that hold the uterus in place. The single continuous sheet of mesothelial cells drapes over the uterus, just like it does every organ that it touches. The uterine ducts and the ovaries and their ligaments (to the uterus, the ovarian ligament; to the sidewall, the suspensory ligament) take up space. But there is a lot of space between the ovary and the pelvic floor from which the uterus arose. That means the single sheet of mesothelium gets really close to itself. The **broad ligament** is the same thing as the **mesentery** and isn't a ligament at all. It is the **lining of the peritoneal cavity as it gets close to itself**. Just like throwing a sheet over a coat rack, where the sheet conforms to the shape of the coat rack and sometimes comes close to itself, so too does the mesothelium conform to the shape of the uterus and sometimes comes close to itself.

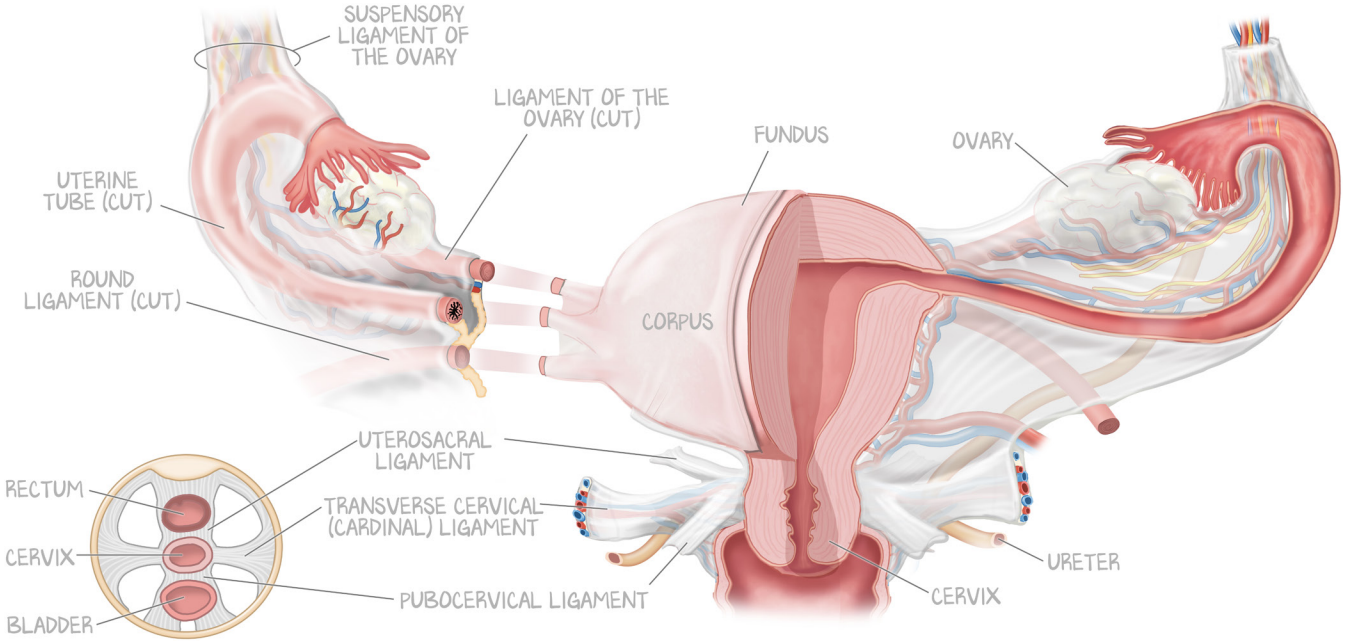

Figure 2.1: Anatomical Relationships in the Pelvis
This depiction is not surgical but akin to a water immersion photograph, wherein the structures appear to be floating rather than pulled down by gravity, to visualize each structure clearly. The uterus proper is the corpus and fundus. It is continuous with the cervix, although we consider the cervix and uterus to be two different organs due to their differing histology and function. The uterine cavity is connected to each ovary via a uterine tube. All of the uterine and ovarian structures are under the peritoneum, which is draped over them. The suspensory ligament of the ovary carries blood vessels, lymphatics, and nerves that supply the uterine tube and ovary and anastomose with the uterine vessels of the transverse cervical ligament. The ligament of the ovary attaches the ovary to the uterus. The round ligament attaches the fundus to the anterior pelvis. The uterosacral ligament connects the cervix to the posterior pelvis, whereas the pubocervical ligament attaches the cervix to the anterior pelvis. The ureters pass by here and a surgeon, looking down at the uterine structures covered by the peritoneum, could easily mistake them for a ligament in the peritoneal cavity.

Vasculature

Embryonically speaking, because all structures develop blood vessels around the same time but then migrate (usually because of the relative migration of other organs dividing and growing larger between structures), structures that developed distant from one another have their own blood supplies, even if they end up right next to each other in the adult. Specifically, the ovaries start at the genital ridge; the uterine tubes, uterus, cervix, and upper third of the vagina start as the Müllerian ducts; and the lower two-thirds of the vagina start as the urogenital sinus. Not surprisingly, the ovaries, uterus, and lower vagina all have their own blood supplies. But because they come together to function as a common unit, it may not be surprising that these blood supplies also anastomose.

Not only are there **three distinct vascular origins**, but also **one continuous anastomotic blood supply** that perfuses the entirety of the female reproductive tract. As with the uterine ligaments, these arteries exist in bilateral pairs, but we describe them singularly.

The ovarian artery travels within the suspensory ligament of the ovary and anastomoses with the Müllerian vascular supply. The distal vagina's vasculature derives from the **internal pudendal** artery and forms an anastomosis with the Müllerian vascular supply. The **Müllerian vasculature** (the blood vessels to the uterus, cervix, and upper third of the vagina) stems from a branch of the internal iliac artery, a common artery that gives rise to the **uterine artery** and its branch, the **vaginal artery**. Use caution here. The internal iliac gives rise to one artery that perfuses the body of the uterus (uterine artery) and that artery has a branch that perfuses the upper third of the vagina (vaginal artery). There are anastomoses

between these branches of the internal iliac artery and between the uterine and ovarian arteries. But the vaginal artery perfuses only the upper third of the vagina, the distal end of the Müllerian ducts. The lower two-thirds of the vagina (discussed in the next lesson) are perfused by a combination of arteries that we want you to learn as simply "the internal pudendal artery." These anastomose with the vaginal and uterine arteries but have a different origin than the Müllerian branches of the internal iliac. The common artery that branches to form both the uterine and vaginal arteries runs within the **transverse cervical ligament**.

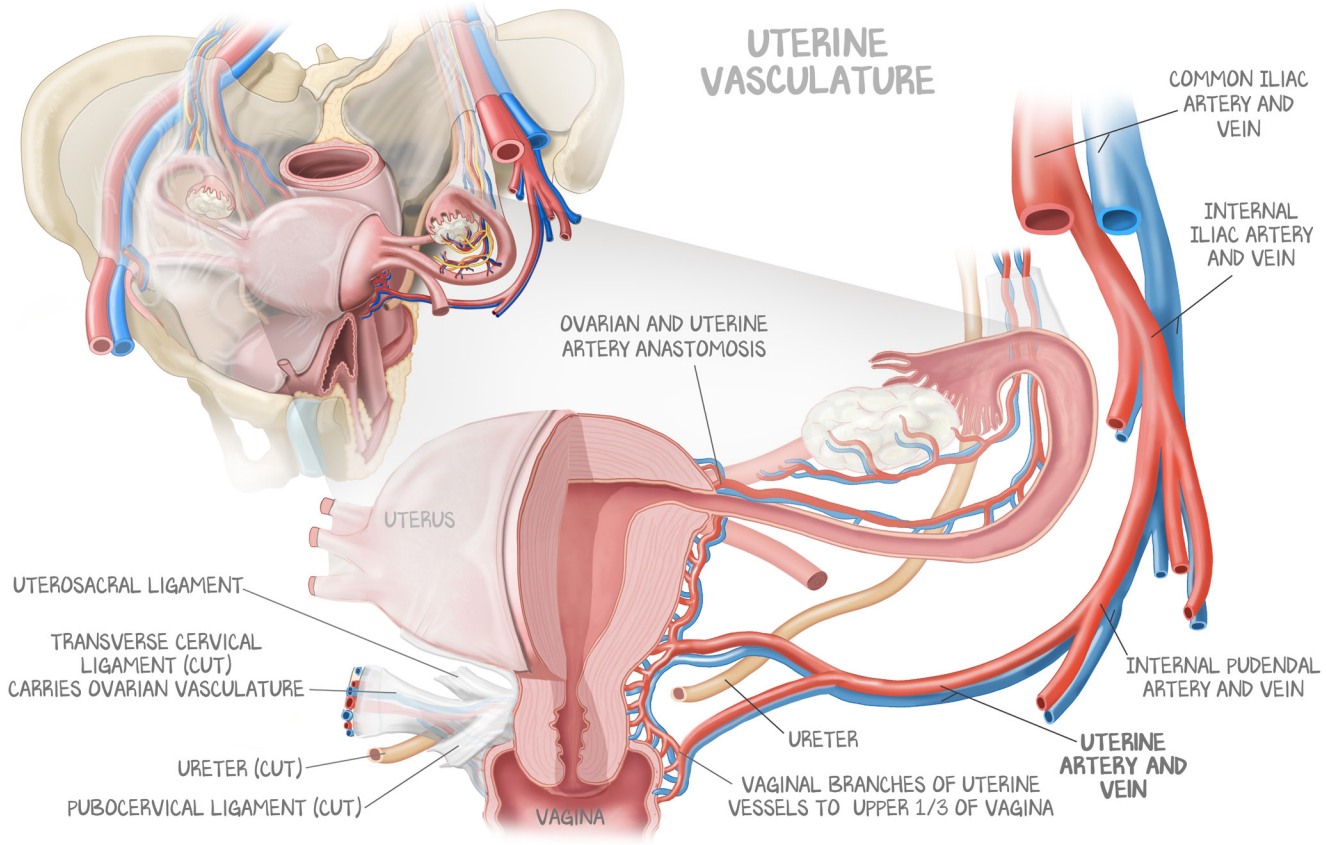

Figure 2.2: Uterine Vasculature Plus
There are two blood supplies to the uterus and uterine tubes. One is derived from branches of the internal iliac artery—the uterine artery to the cervix, the vaginal artery to the upper third of the vagina, then (not shown, as they are vaginal anastomoses) the middle rectal and internal pudendal arteries. The other is the ovarian vasculature within the suspensory ligament of the ovary, which comes from the aorta. The relative anatomy of the cervix, fundus, and uterine tubes and the other pelvic organs (rectum, bladder, urethra) are demonstrated under the peritoneum, as if all the abdominal organs were removed, and you are looking down from within the peritoneal cavity. The artist has purposefully added thickness and translucency to the peritoneum and has illustrated the organs, blood vessels, and ligaments both under the peritoneum (left side) and with the peritoneum resected (right side).

When performing a hysterectomy (from hystera, Greek for "womb"), the surgeon must be sure to **ligate the uterine artery**. The transverse cervical ligament contains the uterine artery. However, ligation of the uterine artery alone may be insufficient to control bleeding. **Anatomic variation** and the **known anastomoses** with the vaginal and ovarian vasculature (not vaginal artery, as ligation of the uterine artery would also ligate the vaginal artery) may necessitate ligation of those arteries. In cases of severe bleeding, temporary ligation of the internal iliac artery may be necessary to prevent exsanguination. Permanent ligation will cause infarction of essentially every visceral organ in the pelvis, but temporary ligation can reduce intraoperative hemorrhage. This is a nod toward the clinical significance of these anastomoses, something we go into much deeper in Clinical Sciences.

Layers of the Uterus

There are three layers of the uterus: endometrium, myometrium, and perimetrium. Oh, whoops—make that two layers, as perimetrium is mesothelium and belongs instead to the peritoneal cavity, or it is "adventitia," which is just the connective tissue between two organs. The two layers of the uterus, then—the endometrium and myometrium— can be explained simply using concepts you already know. The **endometrium** is equivalent to gastric mucosa—an epithelium and a lamina propria. The **epithelium** is "glandular"—**simple columnar epithelium** that invaginates into the lamina propria (just like gastric glands or duodenal crypts). The endometrial glands are just invaginations of simple columnar cells that will secrete the nutrients needed by the embryo after implantation. The lamina propria of the endometrium is called the **stroma**. In the stroma are fibroblast-like cells that can become blood vessels or decidual cells. The **myometrium** is equivalent to the muscularis externa (with inner and outer smooth muscle layers sandwiching a myenteric plexus and blood vessels).

So there are, in fact, three layers to the uterus, but not like most texts teach—the endometrium is an epithelium (1) and stroma (2), and there is a smooth muscle layer called the myometrium (3). This is important because disease stems from an overproliferation of glands (adenomyosis), overproliferation of stroma (uterine polyps), or overproliferation of smooth muscle (uterine leiomyomas, fibroids).

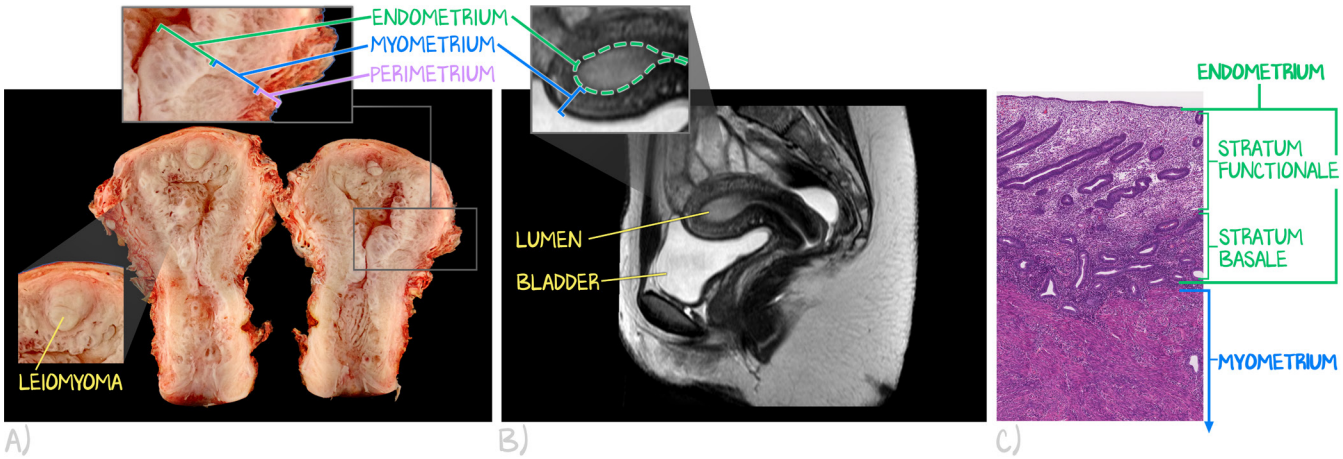

Figure 2.3: Layers of the Uterus
(a) Water immersion photograph (which lifts the endometrium into the uterine cavity) showing the gross layers of the uterus. Despite their different histological appearances, the distinction between the uterus and cervix, as well as the layers of the uterus proper, is not readily apparent on gross inspection. There are blood vessels on the outside (perimetrium), then a seemingly continuous single layer from the perimetrium to the lumen. However, a lighter colored layer exists in the fundus and corpus of the uterus that is not present in the endocervical canal. That lighter layer is the endometrium. The slightly more tan-colored layer is the myometrium. To add more to the confusion, the myometrium is continuous with the stroma of the cervix, which contains very little smooth muscle. (b) T2-weighted MRI showing a similar appearance to the gross specimen. From the inside out, the lightest layer is in the center (lumen), surrounded by a thin rim of dark black (endometrium), and then the rest is grey (myometrium). That arrangement continues into the cervix, where the shades of grey appear nearly identical to those of the corpus and fundus. (c) Histologically, there is a smooth muscle layer (myometrium), a stratum basale that is densely packed with nuclei (endometrium), and a stratum functionale that is less densely packed and has a simple columnar epithelium that invaginates into its stroma to form glands (endometrium).

Then we have to turn to what the layers do **during the uterine cycle**.

The **myometrium doesn't change with the uterine cycle**. It is smooth muscle, so it can contract and relax, facilitating the expulsion of necrotic debris during the menstrual phase of the endometrial cycle if implantation does not occur and getting baby delivered after gestation is complete if implantation does occur. But cycle to cycle, the myometrium (muscularis externa) doesn't vary.

The **endometrium** (uterine mucosa) **changes in response to the ovarian cycle**. We divided the endometrium into epithelium (both the surface epithelium and invaginations to form glands) and stroma. But there is another way to describe the layers of the endometrium. There are the epithelium and stroma of the more basilar **stratum basale** (well named) and the epithelium and stroma of the more apical **stratum functionale**. The epithelium of the stratum basale (simple columnar epithelium that invaginates to form glands) acts as the "stem cell niche" for the epithelium of the stratum functionale, and the stromal cells of the stratum basale act as the "stem cell niche" for the stroma of the stratum functionale. Honestly, it is easier to say that the endometrium of the stratum basale acts as the "stem cell niche" for the endometrium of the stratum functionale, but spelling out epithelium-and-stroma (instead of endometrium) will help you keep straight what happens in health and disease, all of which is to follow in this lesson.

During the **proliferative** phase of the uterine cycle (when the ovarian cycle is in the **follicular phase** and **estrogen** is driving the system), the stratum basale rapidly proliferates, extending the height of the stratum functionale—the stratum basale and functionale are the same continuous epithelium-and-stroma (endometrium). When the stratum basale proliferates, the glands get taller and branch. The stroma must also grow with its epithelium to support it.

Remember the helicine arteries in the corpora cavernosa? They are coiled when flaccid to allow them to stretch out when the penis becomes erect. There's a similar concept here in the uterus. The uterine artery gives off 6–12 **arcuate** arteries that anastomose with each other within the myometrium. Each arcuate artery gives rise to many radial arteries, which become **spiral arteries**. The spiral arteries act as the vascular supply for the endometrium. They are spiral (helicine, coiled, all synonyms) such that as the endometrium proliferates, they can elongate—much like the helicine arteries of the penis. In the uterus, the spiral arteries do not reach the upper third of the proliferative endometrium and instead act as the vessels that feed the arterioles and lacunae in the endometrium. Arterioles lead to capillary beds and sometimes large cavernous spaces lined with endothelial cells. In the uterus, the placenta uses these **lacunae** to establish the maternal-placental circulation. The spiral arteries coil again during menstruation, no longer stretched by the shed endometrium.

If no implantation occurs, the stratum functionale will slough off. Vasoconstriction causes coagulative necrosis, ischemic death of the epithelium and lamina propria. It dies and is lost. As it does, bleeding from the spiral arteries admixes with the shed epithelium, blood vessels, and lamina propria, and the patient has menses, the expulsion of this content.

Phases of the Uterine Cycle, per the Endometrium

There are three continuous phases with no abrupt start or stop, but a gradual transition—proliferative, secretory, and menstrual—dependent on hormonal signals from the ovary. If you understand the ovarian cycle, the uterine cycle is simple—estrogen causes the endometrium to proliferate, progesterone causes the endometrium to secrete, and the absence of both causes the endometrium to slough.

We are going to be repetitive in the following paragraphs so that the last paragraph's final sentence is so innate to you that you're annoyed by reading the same thing a fifth time. Our tale of the uterus begins at ovulation. The estrogen levels climb until the GnRH surge from the hypothalamus leads to the LH surge. The LH surge induces ovulation in one follicle (just one, not one per ovary), and the follicle luteinizes; both the granulosa and theca cells are primed to produce progesterone. Progesterone inhibits the hypothalamus and anterior pituitary, so no FSH is released, so no other follicle grows. We are in the luteal phase of the **ovarian cycle**. The ovary is in control, and the uterus does what it is told. That is, the ovary is the source of endocrine signaling (estrogen, progesterone), and the uterus is the effector organ. The uterus does not participate in endocrine feedback; it merely listens to the ovary's signal. The **uterine**

cycle (colloquially the menstrual cycle) chronologically coincides with the changes in the anterior pituitary and hypothalamus, but the uterine cycle depends on **the ovaries, not the hypothalamic-pituitary axis**. When things go right, the uterine changes overlap changes in FSH and LH, and the erroneous conclusion that the uterus responds to FSH and LH can be drawn. But the uterus listens only to the ovary, and the signals the ovary sends are **estrogen** or **progesterone**.

Now the details of each phase—proliferative, secretory, and menstrual.

In the **proliferative phase**, the cells of the endometrium—epithelium-and-stroma—of the stratum basale proliferate. The stratum functionale rises, enlarging from the basale up as new cells proliferate from the basale. The endometrium gets **taller**. The glands get taller, the stroma gets taller, and new blood vessels form in the rising stroma. Proliferation is driven by **estrogen**.

In the **secretory phase**, the glands that got taller now become active. The endometrium gets **wider**. The glands are lined with secretory ciliated columnar cells. They all secrete the same thing—mucoid fluid with a lot of glycogen. The details are withheld here because they are not relevant. That fluid is the stuff the implanting embryo needs before it can form the maternal-placental connection. And they secrete that stuff into the lumens of the glands—from the surface epithelium to the stratum basale, those glands **engorge**. In addition, some of the stromal cells prepare for the embryo and become **decidual cells**. The exact role of these cells has not been determined, but they are known to be necessary for the successful implantation of an embryo and are often found to be full of glycogen as well. Be careful—the purpose of the *secretory* phase is NOT to secrete the secretions into the uterine lumen but into the glands themselves. The glands become swollen with their secretory product, taking on a corkscrew shape on histology, and the stroma engorges with blood. The secretory phase is induced by **progesterone**.

The switch from estrogen to progesterone is triggered by ovulation. The corpus luteum of the ovary supports progesterone production for approximately 10–14 days. If no implantation occurs, progesterone levels wane. Without estrogen or progesterone, the endothelium sloughs. In the **menstrual phase**, everything shuts off. There is no estrogen to drive proliferation and no progesterone to drive secretion. The spiral arteries contract for hours at a time, resulting in **ischemia** of the stratum functionale. The glands stop secreting. All the new tissue that had proliferated is expelled from the uterus during menses.

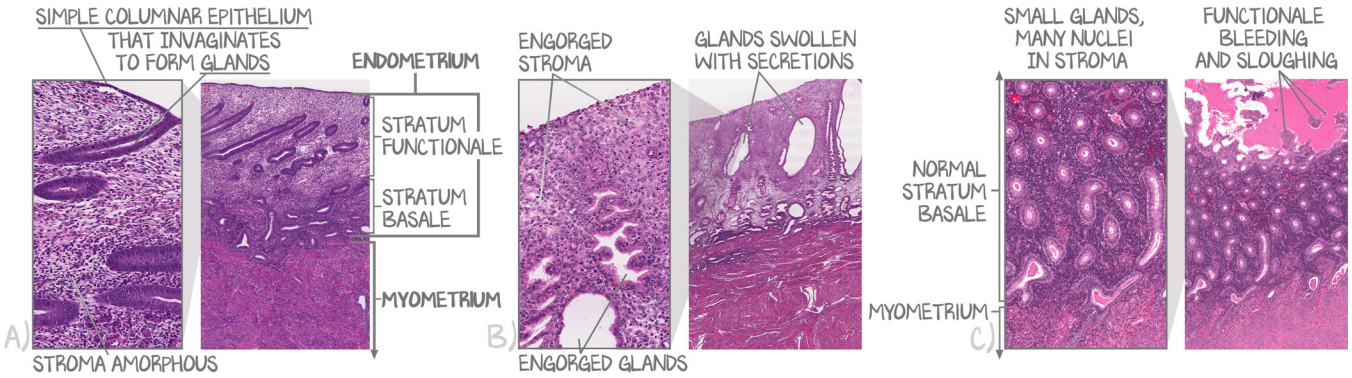

Figure 2.4: Endometrium by Uterine Phases
(a) In the proliferative phase, the stroma and epithelium proliferate. The stratum basale is seen just above the myometrium and has a darker coloration given the density of nuclei (which are difficult to see at this low magnification). The glands are thin (the white lumens barely noticeable), and the stroma of the stratum functionale is less dense than the stratum basale (paler staining). In the magnified figure, the details of the epithelium, glands, and stroma are more easily seen and can be used to compare against subsequent images. (b) In the secretory phase, the ducts become engorged with their own secretions (the white spaces have enlarged and taken on a zig-zag appearance), and the stroma becomes vascularized and edematous. Compare the pale-staining proliferative stroma (where there are nuclei but also a lot of white space) to the stroma in the secretory phase. Although you cannot see the individual cells even on the magnified image, you can tell there is less white space in the stroma, indicating the decidual cells swelling with glycoproteins. (c) The menstrual phase. Embryo implantation did not occur, and there is no β-hCG from the placenta or LH from the anterior pituitary, so the corpus luteum involutes. With that involution, the progesterone signal wanes. Without estrogen or progesterone, the endometrium sloughs off. We see the apical tips fragmenting off and blood (the pink stuff) falling away. At the bottom of the panel, you can see the myometrium. The glands and stroma that remain are the stratum basale.

The mucosa gets taller and puffier, then sloughs off. The mucosa is glandular epithelium—simple columnar epithelium with invaginations—blood vessels, and stromal cells that will become decidual cells.

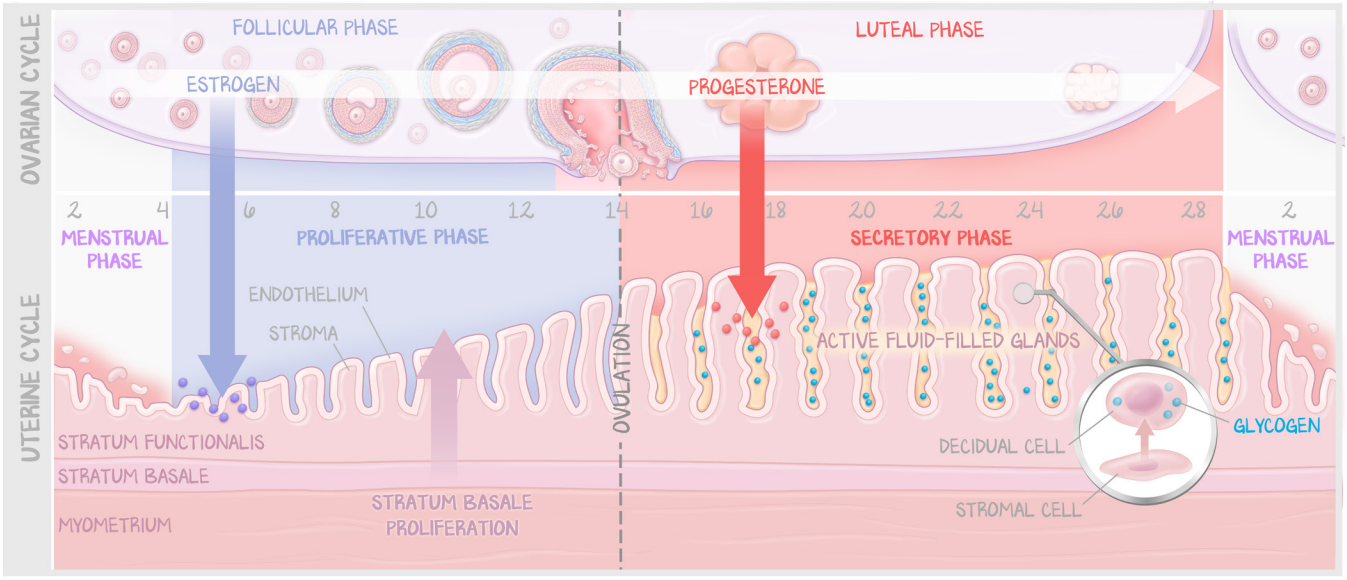

Figure 2.5: The Uterine Cycle
The events in the ovary, ovarian phases, and ovarian hormones are downplayed in this version of Figure 1.14 from the last lesson. We included this image to reinforce that the uterine cycle is wholly dependent on the ovarian cycle. Note that we have included a bit of the myometrium and distinguish the stratum basale from the stratum functionale. Estrogen from the follicular phase of the ovary drives the proliferation of stem cells in the stratum basale. Both the epithelium and the stroma replicate, and as new cells are added rapidly, the stratum functionale rises into the uterine lumen. After ovulation, estrogen production ceases, and proliferation halts. Progesterone from the luteal phase of the ovary induces the glands to secrete a glycoprotein-rich fluid and the stromal cells to become decidual cells, also filled with glycoproteins. If no implantation occurs, without either estrogen or progesterone, the endometrium sloughs off.

An Approach to Abnormal Uterine Bleeding

In the Clinical Sciences, we will introduce the concept of abnormal uterine bleeding—heavy menstrual bleeding (menorrhagia) or intermenstrual bleeding (metrorrhagia)—as symptoms with many etiologies. The patient will present with complaints of bleeding, and it will be your responsibility to work up the patient with abnormal (formerly "dysfunctional") uterine bleeding using the advanced organizer PALM-COEIN ("palm coin").

In the Basic Sciences, we want to use pathology to reinforce histology and physiology, and this lesson is primarily focused on the structure of the uterus. So although it is worthwhile to introduce the organizer now, it isn't how the Basic Sciences are taught. The organizer makes you consider the structural causes of abnormal uterine bleeding (the PALM of PALM-COEIN) versus the nonstructural causes of abnormal uterine bleeding (COEIN). The following table introduces the concept of PALM-COEIN, but we want you focused only on PALM. "P," "A," and "L" are covered in the remaining sections of this lesson—structural causes of abnormal uterine bleeding that are not (pre)malignant. The next lesson's entirety is about "M" (premalignant and malignant causes of abnormal uterine bleeding). COIEN either isn't specific to the Reproduction module or considered in the Clinical Sciences only.

P	Polyp	**C**	Coagulopathy (consider von Willebrand disease)
A	Adenomyosis	**O**	Ovulatory dysfunction (PCOS, menarche, menopause)
L	Leiomyomas	**E**	Endometrial dysfunction (diagnosis of exclusion)
M	Malignancy or endometrial hyperplasia	**I**	Iatrogenic (intrauterine contraceptive device)
		N	Not otherwise specified

Table 2.1: Causes of Abnormal Uterine Bleeding

Structural Problems That Are Not Malignant (PAL)

In this category, learn three conditions: endometrial polyps, adenomyosis, and leiomyomas (also called fibroids). Each condition causes symptoms based on its location. Pain, pain with menstruation (dysmenorrhea), infertility, and other nonspecific complaints may be found. Their size, location, and invasion into the endometrial cavity will dictate the severity of symptoms. Because each diagnosis can have the same symptoms, it becomes more important to identify the things that make each unique—particularly the **physical exam findings** on bimanual examination (a pelvic exam) and **ultrasonographic appearance**. Although MRI is certainly more sensitive and specific, it is often unnecessary. And although transvaginal ultrasound is more invasive than a scanning point-of-care ultrasound, a good pelvic examination and a point-of-care transvaginal ultrasound (during the same examination) can usually provide the answer.

Endometrial polyps are an overgrowth of stromal cells into the uterine lumen, adenomyosis is an overgrowth of glands (simple columnar epithelium that invaginates on itself) in the myometrium, and leiomyomas (fibroids) are an overgrowth of smooth muscle within the myometrium. This is why we had you learn the "three layers" of the uterus as the stroma (polyps), glandular epithelium (adenomyosis), and myometrium (fibroids).

Endometrial polyps are well-circumscribed collections of endometrial tissue within the uterine wall that extend into the uterine lumen. The polyps are made by the **overproliferation of stromal cells**. They are always **benign**. When resected, it appears as though the stromal component of the endometrium has overproliferated, taking whatever glandular epithelium happened to be around it along for the ride. Unless the polyps are very large, the physical exam is unreliable—you can't feel polyps in the uterine

wall. Because they may be pedunculated or sessile, and the nongravid uterine lumen is so small, a transvaginal ultrasound may also miss them. A **saline-infused sonogram** fills the uterine lumen and enables the polyps to float, lifting them off the wall and making them more visible. Most importantly, these are mucosal growths and will not be found in the myometrium, only in the lumen of the uterus.

Adenomyosis is the presence of glandular epithelium (adeno-) within the myometrium (-myosis). And like the "adenos" elsewhere in the course, it isn't glandular like an exocrine gland; it is glandular like an invaginated simple columnar epithelium. Adenomyosis means, "I found endometrium where the myometrium should be." Some texts consider this a variant of endometriosis (what was thought in the 20th century). We do not, nor do most gynecological texts. Adenomyosis is thought to be secondary to overproliferation of the stratum basale (only down into the myometrium, not up to form the stratum functionale). Because it occurs in **women with multiple pregnancies**, and the placenta intentionally burrows into the endometrium, and sometimes into the myometrium, the next cycle finds a gap in the myometrium into which the basale could replicate into. The physical exam will demonstrate a **uniformly boggy uterus**. Boggy generally translates as **enlarged**, specifically **uniformly enlarged**, and **soft**. A transvaginal ultrasound or MRI will confirm, often finding a uniformly distributed endometrium within the myometrium. Because the tissue is responsive to estrogen (as endometrium is supposed to be), medical therapies include GnRH analogs (we're blowing past this without explanation because we will explain it elsewhere) and surgical therapy, including removal of the uterus (hysterectomy).

Leiomyomas are the single most common tumor in women. They are **benign** growths of the smooth muscle of the **myometrium**. Although they exhibit simple chromosomal abnormalities, these growths are **not premalignant**. A very rare cancer, leiomyosarcoma, should always be considered in a patient with leiomyomas, but advanced work-up need not be pursued unless there are extenuating circumstances (which is beyond the scope of Basic Sciences, but you can look forward to more discussion on this in Clinical Sciences). Leiomyomas are common; leiomyosarcoma is not. Leiomyomas are colloquially referred to as **fibroids**. They have the highest incidence in **black women** but can occur in any ethnicity. Although potentially singular, they are often multiple. They are named based on their location relative to the myometrium, endometrium, and "serosa"/"perimetrium." Fibroids can be found in the cervix (cervical fibroids), extend into the "perimetrium" aka the "serosa" (subserosal fibroids), remain beneath the mucosa (submucosal fibroids), and even extend through the mucosa into the uterus (mucosal, meaning into the stroma and epithelium). They can be pedunculated or not. The key for diagnosis is to identify the **nonuniformly enlarged** and **firm** uterus. Ultrasound can facilitate the diagnosis. If leiomyosarcoma is suspected, MRI can distinguish. These are smooth muscle masses, not the endometrial tissue that proliferates and regresses with cycles. However, medical science believes them to be estrogen-responsive because no prepubertal cases have been identified, and **menopause causes them to regress**. However, although hormonal control is an option (such as the GnRH agonists listed above), surgical removal remains the mainstay of treatment. If a woman desires to become pregnant and the leiomyoma is small or easily resected, the tumor alone can be removed (**myomectomy**), or ligation of the arteries leading to the tumor can lead to loss of the tumor alone. If a woman does not desire pregnancy, the leiomyomas are too many in number or too difficult to remove, or there are additional medical benefits of removing the entire uterus (to prevent ongoing anemia caused by bleeding, for example), then total removal of the uterus (total hysterectomy) is indicated.

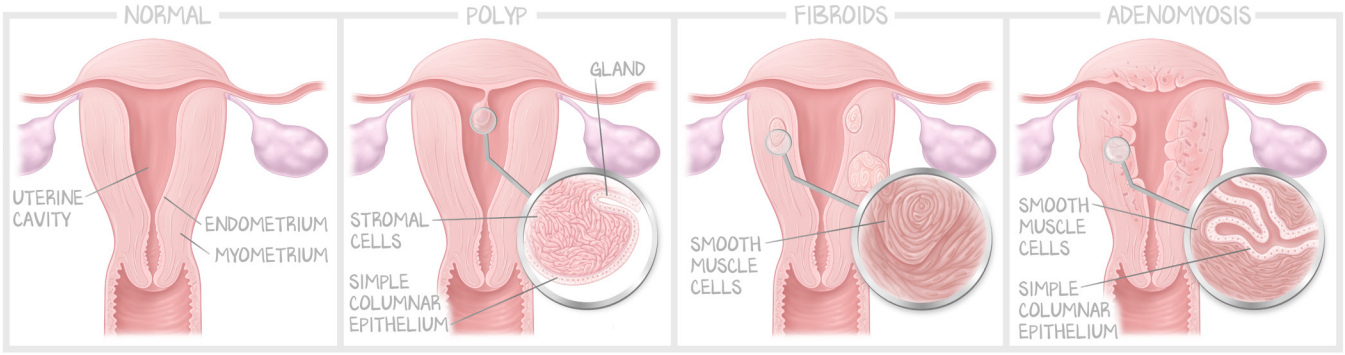

Figure 2.6: Nonmalignant Structural Problems
The normal uterus has a lumen, large myometrium, and endometrium made of both epithelium and stroma. An endometrial polyp is a benign overproliferation of the stromal cells, creating a mass within the uterine lumen. The mass will have surface epithelium and invaginations of that epithelium to form glands, but the stroma-to-gland ratio will be highly increased. Fibroids (leiomyoma) represent an overgrowth of the smooth muscle of the myometrium. Because the myometrium is so large, the growths can push the endometrium into the uterine lumen or push the perimetrium out into the pelvis. Adenomyosis is normal glandular (invaginated simple columnar epithelium) tissue within the myometrium. Whereas the polyps and fibroids are focal, adenomyosis is usually more diffuse.

Structural Problems that Are Malignant (M)

Is the entirety of the next lesson.

The Uterine Tubes

The uterine tubes are extensions of the uterus responsible for sweeping up an ovulated egg, the tubal passageways where fertilization occurs, and how the oocyte gets to the uterine lumen. As ovulation occurs, the uterine tube's most distal end with its large, sweeping, finger-like projections called **fimbriae** comes crashing down on the ovary. The oocyte is out of the ovary and out of the uterus for a brief moment, but the open-ended tube engulfs the ovary, creating a seamless exchange from the ovary to the uterus via the uterine tubes.

Uterine tubes is now the preferred name of these structures. Classically referred to as **fallopian tubes** (having been named by Gabriele Fallopio), we opt to join medical science in removing eponyms and using more descriptive nomenclature. They are also sometimes called **oviducts**, as they are indeed the ducts through which the oocyte travels. However, there is no ovum within the oviducts (only a secondary oocyte or fertilized zygote; see Female Reproduction #5: *Fertilization, Implantation, and Early Embryogenesis*), more than the oocyte travels within the ducts (such as spermatozoa), and the uterine tubes are embryonically distinct from the ovary (the ovary derives from the genital ridge, whereas the uterine tubes and uterus derive from the Müllerian ducts). Thus, we have been using and will continue to use the most appropriate term, uterine tubes.

There are two uterine tubes, one for each ovary. The lumen of the uterine tube is continuous with the lumen of the uterus, as the epithelium is continuous with the endometrium and the smooth muscle layer beneath the epithelium is continuous with the myometrium of the uterus. The epithelium of the uterine tube is **pseudostratified columnar with cilia**. In the uterine tubes, there are papillae, infoldings of the epithelium into the lumen, with a slender lamina propria between rows of pseudostratified columnar epithelium. This epithelium has cilia that sweep the oocyte along the duct and secretory cells that release a fluid that nourishes the oocyte as it passes along.

The uterine tubes are divided into segments, listed in the order the oocyte will encounter them: the infundibulum, ampulla, and isthmus. The **infundibulum** has the largest diameter, the most papillae, and the least amount of smooth muscle. It is the entrance for the egg and what the fimbriae arise from.

The longest portion of the uterine tube is the **ampulla**, the most likely fertilization site to result in successful implantation. Let's say that again, as most texts miss the point of that statement. The ampulla is the longest part of the uterine tube, and the oocyte spends more time here than in either of the other parts, so naturally, this is where there is the highest likelihood of fertilization. But timing matters more than time spent in the ampulla. For implantation to happen, the fertilized embryo must mature to the blastocyst stage. This takes time, and if fertilization happens in the isthmus, there isn't enough time, and the fertilized embryo is passed through the cervical os. If fertilization occurs near the site of ovulation, in the infundibulum, there may be too much embryogenesis; the embryo may become too large and may implant too soon, still within the uterine tubes (called an ectopic pregnancy). So, the ampulla isn't the most common site of fertilization. It is the most common site of fertilization that then goes on to successfully implant.

The portion of the uterine tube with the narrowest lumen and the most smooth muscle is the **isthmus**. Under a microscope and without context, the isthmus looks nearly identical to the ductus deferens of the male spermatic cord, with irregular infoldings of the epithelium into a narrow lumen surrounded by powerful and thick smooth muscle.

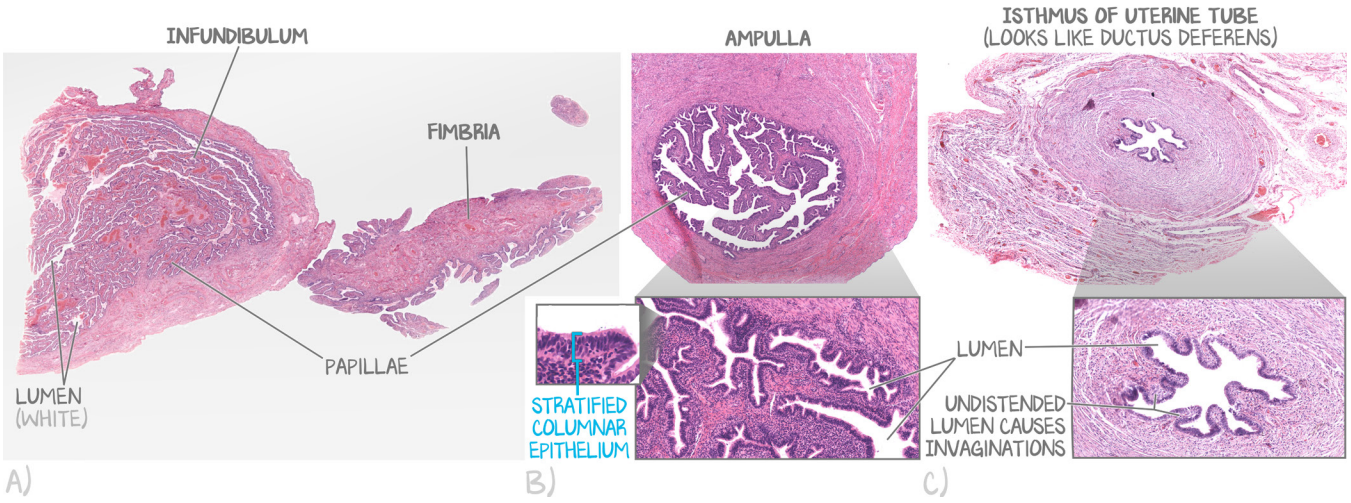

Figure 2.7: The Healthy Uterus
(a) The fimbriae, the wispy projections from the infundibulum, are lined with columnar epithelium. The infundibulum is filled with papillae lined with pseudostratified columnar epithelium, and has the widest diameter and the smallest amount of smooth muscle. The lumen is white, and the papillae are the pink extensions into the lumen. (b) The ampulla has a similar arrangement, smooth muscle on the outside with papillary projections into the lumen. This epithelium is a combination of ciliated and nonciliated pseudostratified columnar cells. (c) The isthmus has the appearance of the ductus deferens, with an enormous amount of smooth muscle surrounding a nondistended lumen. This lack of distention causes invaginations of the simple columnar epithelium into the small lumen. Blood vessels and connective tissue surround the circular muscularis.

Citation

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